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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,095	04/13/2004	Eiichi Ueda	KON-1870	6153

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EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 10/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/824,095	UEDA ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☒ Claim(s) *4 and 7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/04,3/30/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

7DETAILED ACTION

Specification

1. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The recitation of claim 7, 0.11-0.13m is not found in the specification. There are no incidences of liposomes with the diameter in m, which represents meters in the specification and this is assumed to be a typing error.

Claim Objections

2. Claim 4 is objected to because of the following informalities: The instant claim recites "2,4,6-triiodopheny group" which is believed to be a misspelling. Appropriate correction is required.

3. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The instant claim recites "0.11 to 0.13m" which is not further limiting of claim 6 to which is depends.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 10,11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear as to what measure of weight ratio is intended, for example percent weight.

6. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim 25 recites "wherein in step (a), at least one selected from the group consisting of a phospholipid.....etc" whereas step (a) is an active step of mixing a phospholid. As written the instant claim does not define what should be selected from the group and is illogical.

7. Claim 25 recites the limitation "a sterol". There is insufficient antecedent basis for this limitation in the claim. The term sterol is not present in the instant claim 22 to which claim 25 depends.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4,13,17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Mackaness et al. (US 4,192,859).

10. Mackaness et al. (US 4,192,859) teaches of a liposomal X-ray contrast medium having cavities containing the contrast agent therein (column 2, lines 48-52). The contrast agents suitable for use are sodium diatrizoate, iodipamide, iodamide, etc. and are present in 30-50%. The materials constituting the liposome include phospholipids (phosphotidyl choline), sterols (cholesterol) and stearylamine. The organic solvents used to prepare the liposomes include diethyl ether, ethyl acetate that is evaporated under vacuum. The contrast medium is prepared by addition of the liposome to a buffer solution containing iodine containing contrast agent where the contrast agent is trapped within the liposome vesicle (column 3; claims 1-11 and 22).

It is respectfully pointed out that instant claim 2,17 and 18 are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klaveness et al (US 5,676,928) in view of the combined disclosures of Na et al. (US 5,326,552) and Otake et al. (US2004/0099976A1).

13. Klaveness et al (US 5,676,928) discloses a liposomal contrast agent encapsulating an iodine imaging agent for use in X-ray. These unilamellar liposomes have a high encapsulation capacity, 5-6 ml/g and a typical concentration of 10-300mg of encapsulated iodine per ml composition. The iodine imaging agent is contained within the liposome and the liposome suspended in an aqueous medium containing the same iodinated imaging agent and a buffering solution (column 4; column 8, lines 3-9). Any biocompatible gas, such as carbon dioxide, stabilizing agent, such as $EDTANa_2Ca$ or Trometamol may be present (column 6, line 1; column 10, line 23; example 7). The total lipid concentration is generally 20mg/ml to 100mg/ml (column 7, lines 64+). In an effort to obtain the desired particle size, 50nm to 3000nm the liposomes may be passed through a filter with a predetermined pore size (column 9, lines 28-33). The weight ratios and particle size disclosed encompass those of the instant claims. Klaveness et al (US 5,676,928) does not disclose the modification of the phospholipid with a polyalkylene oxide or the preparation of the liposomes with supercritical carbon dioxide.

14. Na et al. (US 5,326,552) discloses nanoparticles containing a 2,4,6-triiodobenzoate X-ray contrast agent where the surface of the nanoparticle is modified by adsorbing a nonionic polyethylene glycol, polyethylene oxide surfactants or block copolymers of propylene oxide and ethylene oxide (claim 4) which are present in the amount of about 0.1-90%, 10-30%, etc. (column 2, lines 42-53; column 4, lines 6-10;

column 6, lines 34-37). The X-ray contrast agent is dispersed in an aqueous liquid that serves as the carrier for the agent (column 4, lines 43-47).

15. Otake et al. (US2004/0099976A1) discloses the use of supercritical carbon dioxide for the preparation of unilamellar liposomes, 50nm to 80nm in diameter that encapsulate a desired substance (p3, [0035]). The liposome preparation involves adding an aqueous solution (to be encapsulated) to a mixture of a phospholipids and/or glycolipid and carbon dioxide under super critical conditions (p1, [0019]-[0020]; p2, [0028]-[0029]). Carbon dioxide under super critical condition is meant to represent carbon dioxide at or above critical temperature (30.98°C) and pressure (7.3773 Mpa) (p2, [0022]).

16. At the time of the invention it would have been obvious to one ordinarily skilled in the art to modify the phospholipids of Klaveness et al (US 5,676,928) with polyalkylene oxides as disclosed by Na et al. (US 5,326,552) to control the interfacial tension between the phospholipids solution and water to facilitate the generation of the liposome vesicle with the desired particle size and it would be obvious to use a commercially available filter with the correct size pores to isolate these desired particles.

17. At the time of the invention it would have been obvious to one ordinarily skilled in the art to prepare this modified liposome via the supercritical carbon dioxide preparation method of Otake et al. (US2004/0099976A1) since it makes it possible to produce these modified unilamellar liposomes with improved trapping efficiency in fewer steps and without using harmful organic solvents.

It is respectfully pointed out that instant claims 2,9 and 17-20 are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 21,22 and 25 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-4,6 and 8 of copending Application No. 11/180849. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: both applications disclose the method of preparing a radiographic contrast medium comprising a unilamellar liposome by mixing a polyalkylene oxide modified phospholipid and a sterol with an aqueous solution containing a water-soluble iodine compound via supercritical carbon dioxide.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

20. Claims 2, 21,22 and 25 are provisionally rejected on the ground of nonstatutory double patenting over claims 1,5,7,11,14-16 and 17 of copending Application No. 11/187397. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: both applications disclose the method of preparing a liposome containing a water-soluble iodine compound, sterols and polyalkylene compounds via supercritical carbon dioxide under increased temperature and pressure. Filtration of the desired iodine containing liposomes is also disclosed in both applications. Further disclosed in both applications is a liposome-containing preparation generated by the method above.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
September 13, 2006

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER